

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Original) Use of a kynurenine 3-hydroxylase inhibitor for the manufacture of a medicament for increasing the number of islets of Langerhans cells.

2. (Original) Use of a kynurenine 3-hydroxylase inhibitor according to Claim 1, in the context of the treatment and/or prevention of diabetes, its complications and/or its related pathologies.

3. (Original) Use of a kynurenine 3-hydroxylase inhibitor for the manufacture of a medicament for the treatment of prediabetes.

4. (Original) Use according to Claim 3, for which the said prediabetes is an insulin-dependent prediabetes.

5. (Original) Use according to Claim 3, for which the said prediabetes is a non-insulin-dependent prediabetes.

6. (Original) Use of a kynurenine 3-hydroxylase inhibitor for the manufacture of a medicament for the treatment and/or prevention of insulin-dependent diabetes.

7. (Original) Use of a kynurenine 3-hydroxylase inhibitor for the manufacture of a medicament for the prevention of non-insulin-dependent diabetes.

8. (Original) Use of a kynurenine 3-hydroxylase inhibitor for the manufacture of a medicament for the treatment of early non-insulin-dependent diabetes.

9. (Currently Amended) Use according to claim 3 ~~any one of Claims 3 to 8~~, for which the said treatment or prevention is by increasing the number of islets of Langerhans cells.

10. (Original) Use of a kynureneine 3-hydroxylase inhibitor in combination with one or more immunosuppressants, for the manufacture of a medicament for the prevention and/or treatment of insulin-dependent diabetes.

11. (Currently Amended) Use according to claim 1 any one of the preceding claims, which is suitable for the said treatment and/or the said prevention in the case of a patient with an impairment in the number of islets of Langerhans cells.

12. (Original) Use according to Claim 11, for which the said patient shows a decrease in the number of islets of Langerhans cells of at least 40%.

13. (Currently Amended) Use according to Claim 11 ~~or 12~~, for which the said patient shows a decrease in the number of islets of Langerhans cells of between 50% and 90%.

14. (Currently Amended) Use according to claim 1 any one of the preceding claims, which is suitable for the said treatment and/or the said prevention in the case of a patient with glucose intolerance.

15. (Original) Use according to Claim 14, for which the said patient presents a fasting glycaemia of between 1.10 g/l and 1.26 g/l and a glycaemia after meals of between 1.40 g/l and 2 g/l after meals.

16. (Currently Amended) Use according to claim 1 any one of the preceding claims, which is suitable for the said treatment and/or the said prevention in the case of a patient with one or more anti-islets of Langerhans cells immunological markers.

17. (Original) Use according to Claim 16, for which the said marker(s) indicate(s) the existence of an autoimmune response of the body directed against the antigenic markers of the body's islets of Langerhans cells.

18. (Currently Amended) Use according to Claim 16 or 17, for which the said marker(s) is (are) chosen from the anti-islet (ICA), anti-glutamic acid decarboxylase (GAD), anti-tyrosine phosphatase (IA-2) and anti-(pro)insulin (AIA) auto-antibodies, or the anti-carboxypeptidase H, anti-64kD and anti-heat shock protein antibodies.

19. (Currently Amended) Use according to claim 1 any one of the preceding claims, which is suitable for the said treatment and/or the said prevention in the case of a patient with insulin resistance.

20. (Original) Use according to Claim 19, for which the said patient responds partially or not at all to insulin secreted by the beta cells or injected.

21. (Currently Amended) Use according to claim 1 any one of the preceding claims, for which the said patient presents a level of glycated haemoglobin of higher than 7%.

22. (Currently Amended) Use according to claim 1 any one of the preceding claims, for which the said patient has islets of Langerhans cells showing an anomaly of insulin secretion in response to glucose.

23. (Currently Amended) Use according to claim 1 any one of the preceding claims, for which the said patient presents a suppression of the early peak of insulin secretion.

24. (Currently Amended) Use according to claim 1 any one of the preceding claims, for which the said patient shows related hyperglycaemia and obesity.

25. (Original) Use according to Claim 24, for which the said patient suffers from paediatric obesity.

26. (Currently Amended) Use according to claim 1 any one of the preceding claims, which is suitable for the said treatment and/or the said prevention in the case of a patient

presenting any diabetic risk factor.

27. (Currently Amended) Use according to Claim 25 or 26, for which the said risk factor is chosen from familial history, gestational diabetes, excess weight, obesity, insufficient physical exercise, high blood pressure, a high level of triglycerides, hyperlipidaemia and inflammation.

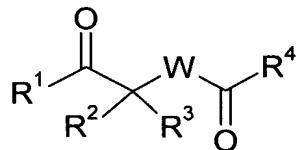
28. (Currently Amended) Use according to claim 1 any one of the preceding claims, comprising the in vitro treatment of isolated islets of Langerhans cells with the said kynurenone 3-hydroxylase inhibitor.

29. (Original) Process for increasing the number or the insulin-secreting capacity of islets of Langerhans cells, comprising the in vitro application of a kynurenone 3-hydroxylase inhibitor to the said cells.

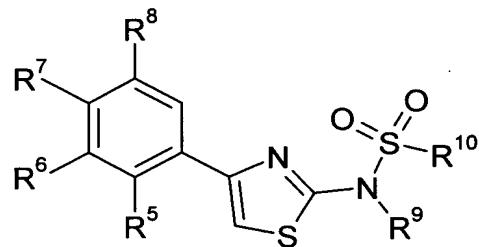
30. (Original) Pharmaceutical composition comprising a kynurenone 3-hydroxylase inhibitor in combination with one or more immunosuppressants.

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33. Use or composition according to claim 1 any one of the preceding claims, for which the said kynurenone 3-hydroxylase inhibitor is a compound of the general formula (I) or (II):



(I)



(II)

in which:

- W represents a divalent radical chosen from the following radicals:



- R<sup>1</sup> represents a radical chosen from linear or branched alkyl containing from 1 to 14 carbon atoms and optionally substituted, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, a heterocyclic radical, an aryl radical and a heteroaryl radical;
- R<sup>2</sup> is chosen from hydrogen, a halogen atom, hydroxyl, thiol, carboxyl, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylcarbonyl, alkoxy carbonyl, aryl, heteroaryl, cycloalkyl and a heterocyclic radical;
- R<sup>3</sup> is chosen from hydrogen, a halogen atom, hydroxyl, thiol, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, aryl, heteroaryl, cycloalkyl and a heterocyclic radical;
- R<sup>2</sup> and R<sup>3</sup> together also possibly forming a group =CR<sup>16</sup>R<sup>17</sup>; or alternatively together forming, with the carbon atom that bears them, a cycloalkyl radical or a heterocyclic radical;
- R<sup>4</sup> is chosen from hydroxyl, alkoxy, alkenyloxy, alkynyoxy, aryloxy, heteroaryloxy, -N(R<sup>12</sup>R<sup>12'</sup>), -N(R<sup>12</sup>)OR<sup>13</sup>, linear or branched alkyl containing from 1 to 14 carbon atoms and optionally substituted, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl and a heterocyclic radical;
- R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup> and R<sup>8</sup>, which may be identical or different, are chosen, independently of each other, from hydrogen, a halogen atom, and a nitro, cyano, hydroxyl, trifluoromethyl, alkyl, alkoxy, cycloalkyl or aryl radical;
- the radicals R<sup>5</sup> and R<sup>6</sup>, on the one hand, or R<sup>6</sup> and R<sup>7</sup>, on the other hand, may also form, together with the carbon atoms to which they are attached, a benzene ring optionally substituted by one or more groups, which may be identical or different, chosen from a halogen atom, a trifluoromethyl, cyano or nitro radical, an alkyl radical and an alkoxy radical;
- R<sup>9</sup> represents hydrogen or an alkyl radical;
- R<sup>10</sup> is chosen from an alkyl, an aryl and a heteroaryl radical;
- R<sup>12</sup> and R<sup>12'</sup>, which may be identical or different, are chosen, independently of each other, from hydrogen and an alkyl, alkenyl, alkynyl, alkylcarbonyl, aryl or heteroaryl radical; or alternatively R<sup>12</sup> and R<sup>12'</sup> may form, together with the nitrogen atom to which they are attached, a monocyclic or bicyclic heterocyclic group containing a total of 5 to 10 atoms, among which 1, 2, 3 or 4 are chosen, independently of each other, from nitrogen, oxygen and sulfur, the said

heterocyclic radical also optionally comprising 1, 2, 3 or 4 double bonds and optionally being substituted by one or more chemical groups, which may be identical or different, chosen from hydroxyl, halogen atom, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, aryl, heteroaryl, heterocyclic radical and trifluoromethyl;

- R<sup>13</sup> is chosen from hydrogen and an alkyl, alkenyl, alkynyl, aryl, heteroaryl, -N(R<sup>12</sup>R<sup>12</sup>) or -N(R<sup>12</sup>)OR<sup>13</sup> radical;
- R<sup>14</sup> is chosen from hydrogen, a halogen atom, hydroxyl, thiol, carboxyl, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylcarbonyl, alkoxy carbonyl, aryl, arylalkyl, heteroaryl, cycloalkyl and a heterocyclic radical;
- R<sup>14</sup> may also form a bond with R<sup>2</sup>, thus forming a double bond between the carbon atoms respectively bearing the substituents R<sup>14</sup> and R<sup>2</sup>; or alternatively R<sup>14</sup> forms, with R<sup>2</sup> and with the carbon atoms that bear them, a ring containing a total of 3, 4, 5, 6 or 7 carbon atoms, among which 1, 2 or 3 may be replaced with an atom chosen from nitrogen, oxygen and sulfur, the said ring possibly comprising one or more unsaturations in the form of (a) double bond(s), and being optionally substituted by one or more radicals, which may be identical or different, chosen from oxo, alkoxy, alkoxy carbonyl and alkylcarbonyloxy;
- R<sup>15</sup> is chosen from hydrogen, a halogen atom, hydroxyl, thiol, carboxyl, alkyl, alkenyl, alkynyl, alkylcarbonyl, alkoxy carbonyl, alkoxy, alkenyloxy, alkynyoxy, aryloxy, cycloalkyloxy, heteroaryloxy, heterocyclyloxy, alkylthio, alkenylthio, alkynylthio, arylthio, cycloalkylthio, heteroarylthio, heterocyclthio, aryl, heteroaryl, cycloalkyl and a heterocyclic radical;
- R<sup>14</sup> and R<sup>15</sup> also possibly forming, together with the carbon atom that bears them, a cycloalkyl radical or a heterocyclic radical;
- R<sup>16</sup> and R<sup>17</sup>, which may be identical or different, are chosen, independently of each other, from hydrogen, a halogen atom, an alkyl, aryl, heteroaryl or cycloalkyl radical and a heterocyclic radical; or alternatively
  - R<sup>16</sup> and R<sup>17</sup> form, together with the carbon atom that bears them, a cycloalkyl radical or a heterocyclic radical; and
  - R<sup>11</sup> is chosen from hydrogen and an alkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl or cycloalkylalkyl radical, and any protecting group for an amine function;

and also the possible geometrical and/or optical isomers thereof, and possible tautomeric forms thereof;

the solvates and hydrates of these compounds;

and also the possible salts thereof with a pharmaceutically acceptable acid or base, or alternatively the pharmaceutically acceptable prodrugs of these compounds.

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53. Process for manufacturing a medicament for the treatment and/or prevention of diabetes, its complications and/or its related pathologies, by increasing the number of islets of Langerhans cells, in which at least one compound of the formula (I) or (II) as defined in one of claim 1 ~~Claims 1 to 34~~ is subjected to an *in vitro* test of inhibition of kynurenine 3-hydroxylase, and the molecules responding positively to the said tests are then conditioned in the form of a pharmaceutical composition, optionally with addition of a pharmaceutically acceptable filler or vehicle.

54. Process for screening candidate compounds for activity in the prevention or treatment of diabetes, its complications and/or its related pathologies, by increasing the number of islets of Langerhans cells by inhibiting kynurenine 3-hydroxylase, the said candidates not corresponding to formula (I) or (II) as defined in one of claim 33 ~~Claims 33 to 51~~, in which process the candidate compounds are subjected to an *in vitro* test of inhibition of kynurenine 3-hydroxylase, and the candidate that has responded positively to this test is selected.